IN THE CLAIMS

1. (Currently amended) A bisubstrate inhibitor of insulin receptor kinase, comprising:

a nucleotide or nucleotide analog moiety comprising a triphosphate; and

a peptide moiety which is a substrate for said insulin receptor kinase and which comprises a tyrosine residue or a 2-amino-3-(4-amino-phenyl)-propionic acid residue;

wherein said moieties are linked by a tether ~~that comprises a proton donor~~, wherein said tether is linked to the tyrosine residue via its phenolic oxygen or to the 2-amino-3-(4-amino-phenyl)-propionic acid residue via its aniline nitrogen and wherein said tether is linked to the nucleotide or nucleotide analog moiety via the gamma phosphate of the triphosphate, wherein the tether is [[≥]] greater than or equal to 4.9 Å measured from a gamma phosphorus of the nucleotide or nucleotide analog moiety to a ~~the~~ proton donor of the tether formed by the phenolic oxygen or the aniline nitrogen.

2. (Original) The bisubstrate inhibitor of claim 1 wherein the nucleotide or nucleotide analog moiety is ATP.

3. (Original) The bisubstrate inhibitor of claim 1 wherein the nucleotide or nucleotide analog moiety is γ-S-ATP.

4. (Currently amended) The bisubstrate inhibitor of claim 1 wherein the peptide comprises a 2-amino-3-(4-amino-phenyl)-propionic acid residue ~~tyrosine residue in which its phenolic oxygen is replaced with a nitrogen atom~~.

5. (Currently amended) The bisubstrate inhibitor of claim 1 wherein the peptide moiety has at least 4 contiguous amino acid residues selected from the sequence Lys Lys Lys Leu Pro Ala Thr Gly Asp Tyr Met Asn Met Ser Pro Val Gly Asp ~~Lys, Lys, Lys, Leu, Pro, Ala, Thr, Gly, Asp, Tyr, Met, Asn, Met, Ser, Pro, Val, Gly, Asp~~ (SEQ ID NO:1).

6. (Currently amended) The bisubstrate inhibitor of claim 1 wherein the peptide moiety has at least 5 contiguous amino acid residues selected from the sequence Lys Lys Lys Leu Pro Ala Thr Gly Asp Tyr Met Asn Met Ser Pro Val Gly Asp ~~Lys, Lys, Lys, Leu, Pro, Ala, Thr, Gly, Asp, Tyr, Met, Asn, Met, Ser, Pro, Val, Gly, Asp~~ (SEQ ID NO:1).

7. (Currently amended) The bisubstrate inhibitor of claim 1 wherein the peptide moiety comprises the sequence Lys Lys Lys Leu Pro Ala Thr Gly Asp Tyr Met Asn Met Ser Pro Val Gly Asp ~~Lys, Lys, Lys, Leu, Pro, Ala, Thr, Gly, Asp, Tyr, Met, Asn, Met, Ser, Pro, Val, Gly, Asp~~ (SEQ ID NO:1).

8. (Original) The bisubstrate inhibitor of claim 1 wherein the nucleotide or nucleotide analog moiety is a nucleotide in which one or more phosphate groups are replaced by uncharged alkyl groups.

9. (Original) The bisubstrate inhibitor of claim 1 wherein the nucleotide or nucleotide analog moiety is a nucleotide in which one or more phosphate groups are replaced by uncharged C_1 to C_3 alkyl groups.

10. (Original) The bisubstrate inhibitor of claim 1 wherein the peptide moiety comprises a membrane translocating sequence (MTS).

11. (Original) The bisubstrate inhibitor of claim 10 wherein the MTS is at the N-terminus of the peptide moiety.

12. (Original) The bisubstrate inhibitor of claim 10 wherein the MTS is at the C-terminus of the peptide moiety.

13. (Original) The bisubstrate inhibitor of claim 1 wherein the peptide moiety comprises an HIV TAT sequence.

14. (Original) The bisubstrate inhibitor of claim 1 wherein the peptide moiety comprises carbon-carbon bonds in place of amide bonds.

15. (Currently amended) A bisubstrate inhibitor of insulin receptor kinase, comprising:

a nucleotide or nucleotide analog moiety;

and a peptide moiety which is a substrate for said insulin receptor kinase;

wherein said moieties are linked by a tether that comprises a proton donor, wherein the tether is [[≥]] greater than or equal to 4.9 Å measured from a gamma phosphorus of the nucleotide or nucleotide analog moiety to the proton donor, wherein the bisubstrate inhibitor of insulin receptor kinase is Compound 2.

16-57. (Canceled)

58. (Original) The bisubstrate inhibitor of claim 1 which is bound to insulin receptor kinase.

59. (Canceled)

60. (Currently amended) A bisubstrate inhibitor of a protein kinase comprising:

a nucleotide or nucleotide analog moiety comprising a triphosphate; and

a peptide moiety which is a substrate for said protein kinase and which comprises a tyrosine residue, a 2-amino-3-(4-amino-phenyl)-propionic acid residue, a serine residue, a 2,3-diamino-propionic acid residue, a threonine residue, or a 2,3-diamino-butyric acid residue;

wherein said moieties are linked by a tether ~~that comprises a proton donor~~, wherein said tether is linked to the tyrosine residue via its phenolic oxygen, to the 2-amino-3-(4-amino-phenyl)-propionic acid residue via its aniline nitrogen, to the serine residue via its hydroxyl oxygen, to the 2,3,diamino-propionic acid residue via its 3-amino nitrogen, to the threonine residue via its hydroxyl oxygen, or to the 2,3-diamino-butyric acid via its 3-amino nitrogen, and wherein said tether is linked to the nucleotide or nucleotide analog moiety via the gamma phosphate of the triphosphate, wherein the tether is [[≥]] greater than or equal to 4.9 Å measured from a gamma phosphorus of the nucleotide or nucleotide analog to a ~~the~~ proton donor of the tether formed by the phenolic oxygen, the aniline nitrogen, the hydroxyl oxygen, or the 3-amino nitrogen.

61. (Canceled)

62. (Canceled)

63. (Currently amended) The bisubstrate inhibitor of claim 60 wherein the protein kinase is a tyrosine protein kinase and the peptide comprises a tyrosine residue.

64. (Canceled)

65. (Canceled)

66. (Currently amended) The bisubstrate inhibitor of claim 63 wherein a nitrogen atom replaces a hydroxyl oxygen on the [[a]] tyrosine.

67. (Original) The bisubstrate inhibitor of claim 60 which is bound to the protein kinase.

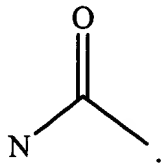
68. Canceled)

69. (Previously presented) The bisubstrate inhibitor of claim 60 wherein the peptide moiety comprises at least 4 contiguous amino acids of a natural substrate of said protein kinase.

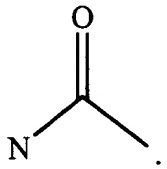
70. (Previously presented) The bisubstrate inhibitor of claim 60 wherein the peptide moiety comprises at least 5 contiguous amino acids of a natural substrate of said protein kinase.

71. (Previously presented) The bisubstrate inhibitor of claim 60 wherein the peptide moiety comprises at least 6 contiguous amino acids of a natural substrate of said protein kinase.

72. (Previously presented) The bisubstrate inhibitor of claim 1 wherein the tether is



73. (Previously presented) The bisubstrate inhibitor of claim 60 wherein the tether is



74. (Previously presented) The bisubstrate inhibitor of claim 60 wherein the peptide moiety is a natural substrate of said protein kinase.

75. (Previously presented) The bisubstrate inhibitor of claim 60 wherein the nucleotide or nucleotide analog moiety is a substrate for said protein kinase.

76. (Previously presented) The bisubstrate inhibitor of claim 1 wherein the nucleotide or nucleotide analog moiety is a substrate for said insulin receptor kinase.